Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Recommendations from the EGAPP Working Group: routine testing for Factor V Leiden (R506Q) and prothrombin (20210G>A) mutations in adults with a history of idiopathic venous thromboembolism and their adult family members.

Bibliographic Source(s)

Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group. Recommendations from the EGAPP Working Group: routine testing for Factor V Leiden (R506Q) and prothrombin (20210G>A) mutations in adults with a history of idiopathic venous thromboembolism and their adult family members. Genet Med. 2011 Jan;13(1):67-76. [55 references] PubMed

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Summary of Recommendations

The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group found adequate evidence to recommend against routine testing for Factor V Leiden (FVL) and/or prothrombin 20210G>A (PT) in the following circumstances: (1) adults with idiopathic venous thromboembolism (VTE). In such cases, longer term secondary prophylaxis to avoid recurrence offers similar benefits to patients with and without one or more of these mutations. (2) Asymptomatic adult family members of patients with VTE and an FVL or PT mutation, for the purpose of considering primary prophylactic anticoagulation. Potential benefits are unlikely to exceed potential harms. The overall certainty of these findings was deemed "moderate." The evidence was insufficient to determine whether FVL/PT testing might have clinical utility in some circumstances, such as for identifying FVL homozygosity among asymptomatic family members of adults with idiopathic VTE or counseling patients about the risks and benefits of antithrombotic therapy. Based on the available evidence, the certainty of net health benefit was deemed "low." The recommendations do not extend to patients with other risk factors for thrombosis, such as contraceptive use, as the evidence review that serves as the basis for the recommendations focused primarily on idiopathic VTE.

Rationale

In developing these recommendations the EGAPP Working Group considered evidence in the following three areas.

Analytic Validity

There is adequate evidence that testing accurately and reliably detects the R506Q (FVL) and 20210G>A (PT) variants in the Factor V and PT

genes, respectively (a more complete definition of analytic validity, clinical validity, and clinical utility is contained under the "Clinical Considerations" section).

Clinical Validity

The presence of a heterozygous FVL variant seems to be a weak risk factor for recurrence of VTE odds ratio [OR]: 1.56). Rare homozygous FVL mutations present somewhat greater risks of VTE recurrence (OR: 2.65). The evidence for this increased risk is convincing, but the magnitude of excess risk is not as great as previously thought. The evidence is insufficient to draw conclusions about excess VTE recurrence risk resulting from compound heterozygosity (FVL and PT), but it is likely to be at least as high as with FVL alone. The OR for compound heterozygosity is 6.69. The evidence is insufficient to draw conclusions about VTE recurrence risks associated with PT mutations alone. For family members of index VTE cases, there is convincing evidence that both heterozygosity and homozygosity for FVL are associated with higher risks for VTE occurrence (ORs 3.49 and 17.84, respectively) than for family members without FVL variants.

Clinical Utility

There is convincing evidence that longer term secondary prophylaxis after an initial idiopathic VTE event yields comparable benefits to those with and without a FVL or PT mutation. For asymptomatic family members of index cases, no prophylaxis trials have been reported. Hence, there is no direct evidence of particular benefit to family members. Potential net harm is possible if primary prophylaxis is administered to asymptomatic family members with one or more mutations, because the absolute risk of an initial VTE event is low, and the risk of anticoagulant-induced hemorrhage is relatively high.

Clinical Considerations

Definitions Used by Evaluation of Genomic Applications in Practice and Prevention

- Factor V Leiden (FVL; R506Q), the most common known inherited risk factor for thrombosis, results from a base change from G to A at position 1691 of the gene encoding coagulation Factor V. The associated amino acid substitution eliminates one of three activated Protein C cleavage sites in the Factor V protein, resulting in Factor V being inactivated more slowly and generating more thrombin, thereby enhancing the potential for clot formation.
- Prothrombin (PT; 20210G>A), the second most common known inherited risk factor for thrombosis, is a gene variant that produces an amino acid substitution in the PT protein, which results in higher circulating PT levels and an enhanced potential for clot formation.
- Venous thromboembolism (VTE), including deep venous thrombosis and pulmonary embolism, is characterized by pathologic thrombosis occurring in the venous circulatory system. The present report deals with idiopathic VTE (also referred to as "unprovoked" VTE), meaning that the event occurs in the absence of a known precipitating factor, such as oral contraceptives, surgery, trauma, or cancer.
- Thrombophilia refers to an acquired or inherited condition that predisposes to the development of pathologic thromboses.
- Analytic validity refers to the ability of a test to accurately and reliably measure the genotype or analyte of interest, in this case the above-described mutations in Factor V and PT genes.
- Clinical validity is defined as a test's ability to accurately and reliably identify or predict the disorder or phenotype of interest, in this case the ability of FVL and PT mutation testing to predict occurrence or recurrence of VTE.
- Clinical utility defines the balance of benefits and harms associated with the use of the test in practice, including improvement in measurable clinical outcomes and usefulness/added value in clinical management and decision making, compared with not using the test. In the present context, clinical utility depends on the extent to which identification of a FVL or PT mutation alters management in index cases with VTE and leads to health-related outcomes that are significantly improved over current practice. Among family members of index cases, clinical utility again depends on the extent to which management changes when a mutation is identified and most importantly how effectively such management leads to avoidance of VTE. A test may be found to have clinical validity (i.e., be a legitimate risk factor for the disorder) without having clinical utility if there is not sufficient evidence to show benefits resulting from use of the test. In the present context, clinical utility of FVL and PT will depend on whether their identification affects patient management and outcome.

Patient Population Under Consideration

These recommendations apply to adults with a history of idiopathic VTE and their asymptomatic adult family members. The recommendations do not extend to individuals with other known risk factors for thrombosis, such as contraceptive use.

Contextual Issues Important to the Recommendation

Cost-Effectiveness

- Cost-effectiveness modeling studies in this area require updating with current VTE risk estimates but are suggestive that routine FVL/PT testing is not cost-effective.

Definitions:

Recommendations Based on Certainty of Evidence, Magnitude of Net Benefit, and Contextual Issues

High or Moderate	Recommend for: • If the magnitude of net benefit is Substantial, Moderate, or Small, unless additional considerations warrant caution. • Consider the importance of each relevant contextual factor and its magnitude or finding. Recommend against: • If the magnitude of net benefit is Zero or there are net harms. • Consider the importance of each relevant contextual factor and its magnitude or finding.
Low	Insufficient evidence: • If the evidence for clinical utility or clinical validity is insufficient in quantity or quality to support conclusions or make a recommendation. • Consider the importance of each contextual factor and its magnitude or finding. • Determine whether the recommendation should be Insufficient (neutral), Insufficient (encouraging), or Insufficient (discouraging). • Provide information on key information gaps to drive a research agenda.

Teutsch SM, Bradley LA, Palomaki GE, Haddow JE, Piper M, Calonge N, Dotson WD, Douglas MP, Berg AO; EGAPP Working Group. The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) initiative: methods of the EGAPP Working Group. Genet Med. 2009 Jan;11(1):3-14.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Idiopathic venous thromboembolism (VTE)

Guideline Category

Evaluation

Management

Prevention

Risk Assessment

Technology Assessment

Clinical Specialty

Family Practice

Hematology

Internal Medicine

Medical Genetics

Preventive Medicine

Intended Users

Advanced Practice Nurses

Health Care Providers

Health Plans

Managed Care Organizations

Physician Assistants

Physicians

Utilization Management

Guideline Objective(s)

To address whether Factor V Leiden (FVL) testing alone, or in combination with prothrombin G20210A testing, leads to improved clinical outcomes in adults with a personal history of venous thromboembolism (VTE) or to improved clinical outcomes in adult family members of mutation-positive individuals

Target Population

Adults with a history of idiopathic venous thromboembolism and their asymptomatic adult family members

Note: The recommendations do not extend to individuals with other known risk factors for thrombosis, such as contraceptive use.

Interventions and Practices Considered

Routine genetic testing for the presence of Factor V Leiden (R506Q) and prothrombin (20210G>A) mutations

Major Outcomes Considered

Analytic Validity

Reliability of genetic testing to identify Factor V Leiden (R506Q) and prothrombin 20210G>A mutations

Clinical Validity

Reliability of detection of the above mutations to predict recurrence of venous thromboembolism (VTE) in index cases and occurrence in asymptomatic family members

Clinical Utility

- Behavior/treatment patterns
    - Physician use of test results

    - Physician confidence in mutation testing
    - Uptake of mutation testing
- Recurrence rate of VTE during anticoagulation therapy

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) commissioned an evidence review, which was conducted by investigators at the Johns Hopkins University Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD.

Key Questions Relating to the Analytic Framework

The overarching question (Key Question [KQ] 1) was: Does Factor V Leiden (FVL) testing, alone or in combination with prothrombin G20210A testing, lead to improved clinical outcomes (e.g., avoidance of a recurrent venous thromboembolism [VTE]) in adults with a personal history of VTE or to improved clinical outcomes (e.g., avoidance of an initial VTE) in adult family members of mutation-positive individuals? Are testing results useful in medical, personal, or public health decision making? To address this question, investigators reviewed the literature regarding these tests' analytic validity, clinical validity, and clinical utility when used in probands with VTE and in their family members.

The other KQs were as follows:

- KQ2 What is the evidence regarding the analytic validity of existing diagnostic tests for the FVL mutation and the prothrombin G20210A mutation, specifically their analytic sensitivity and specificity, reproducibility, and robustness (sources of variability)?
- KQ3a What is the evidence that the presence of FVL alone, prothrombin G20210A alone, or the two in combination predicts the risk of recurrent VTE in individuals (probands) who have had VTE and predicts the risk of VTE in the probands' family members who have been tested? Does the testing add predictive information beyond clinical data?
- KQ3b What is the evidence that demographic or clinical factors modify the relationship between the presence of FVL or prothrombin G20210A and the risk of VTE?
- KQ4a What is the evidence that clinicians manage patients differently based on the results of testing for FVL or prothrombin G20210A? How do clinicians manage anticoagulation of individuals who have had testing, as compared to those who have not had testing? What other diagnostic tests do clinicians order or not order, based on testing results? What recommendations do clinicians make regarding other therapies and exposures, based on testing results?
- KQ4b What is the evidence that testing, and the resultant management, reduces VTE related outcomes or has other benefits in individuals who have had VTE or in the probands' family members who have been tested?
- KQ4c What is the evidence of harms to individuals with VTE or to the probands' family members who are tested for FVL or prothrombin G20210A as a result of testing or as a result of changed management based on the test results?
- KQ4d What is the evidence that testing for FVL alone, prothrombin G20210A alone, or the two tests in combination is a cost-effective strategy when caring for a patient with VTE or a family member of a proband?

Literature Search

The comprehensive search included electronic and hand searching. Five databases, MEDLINE® (1950 through May 2008), EMBASE® (1974 through December 2008), The Cochrane Library (Issue 2, 2008), the Cumulative Index to Nursing & Allied Health Literature (CINAHL®; 1982 through December 2008) and PsycINFO©, were searched to identify primary literature on the analytic validity, clinical validity, and clinical utility of testing for FVL and prothrombin G20210A.

Two independent reviewers, from among six study team members, conducted title scans in parallel. The title review was designed to capture as many studies as possible that reported on the analytic validity, clinical validity, and clinical utility of testing for FVL and prothrombin G20210A. All titles potentially addressing these issues were promoted to the abstract review phase.

Abstracts were reviewed independently by two investigators. Abstracts were excluded if the investigators agreed that the article: (1) was not relevant to any of the key questions; (2) did not include any human data; (3) contained no original data; (4) was not conducted in adults; and (5) was not published in English. Differences of opinion were resolved through consensus adjudication.

Full articles selected for review underwent another independent parallel review by two investigators. In addition to the exclusion criteria used for the abstract review, there were additional exclusion criteria for each KQ. For the question about clinical validity of the mutations (KQ 3), only prospective studies of probands were included, although retrospective studies of family members were permitted because few prospective studies were anticipated.

Number of Source Documents

7,777 titles were reviewed and 124 articles were included in the review of one or more of the Key Questions.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

(1) "High" grade, indicating confidence that further research is very unlikely to change confidence in the estimated effect in the abstracted literature

(2) "Moderate" grade, indicating that further research is likely to have an important impact on confidence in the estimates of effects and may change the estimates in the abstracted literature

(3) "Low" grade, indicating that further research is very likely to have an important impact on confidence in the estimates of effects and is likely to change the estimates in the abstracted literature

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) commissioned an evidence review, which was conducted by investigators at the Johns Hopkins University Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD.

Each article underwent double review by study investigators for full data abstraction and assessment of study quality. A sequential review process in which the primary reviewer completed all data abstraction forms was used, and the second reviewer checked the first reviewer's data abstraction forms for completeness and accuracy. Reviewer pairs were formed to include personnel with both clinical and methodological expertise. All information from the article review process was entered directly into the SRS 4.0 database.

The primary outcome extracted from the studies of analytic validity was concordance between the test and the reference test, as that was most often reported. When there were sufficient data (three or more studies) and the studies were qualitatively homogeneous with respect to key variables (population characteristics, study duration, mutation status, and length of follow-up), meta-analyses for the studies was conducted addressing the clinical validity of the tests. When it was inappropriate to combine studies quantitatively, the results were qualitatively summarized. For pooling, the number of events and a count of the patients under observation in each group were used. A pooled estimate of the odds ratio for venous thromboembolism (VTE) in probands and separately in family members was calculated. A random effects model was used with the DerSimonian and Laird method for calculating between-study variance.

At the completion of the review, the quantity, quality, and consistency of the best available evidence addressing the key questions was graded by adapting an evidence-grading scheme recommended by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group. To assess the quantity of evidence, the investigators focused on the number of studies with the strongest design. The investigators also assessed the quality and consistency of the best available evidence, including assessment of the limitations affecting individual study quality (using the individual study quality assessments), certainty regarding the directness of the observed effects in the studies, the precision and strength of the findings, and the availability (or lack) of data to answer the key questions.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) commissioned an evidence review, which was conducted by investigators at the Johns Hopkins University Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD.

EGAPP is a project developed by the Office of Public Health Genomics at the Centers for Disease Control and Prevention to support a rigorous, evidence-based process for evaluating genetic tests and other genomic applications being proposed (or used in) clinical and public health practice in the United States. A key goal of the EWG is to develop conclusions and recommendations regarding clinical genomic applications and to establish clear linkage to the supporting scientific evidence. The EWG members are nonfederal multidisciplinary experts convened to establish methods and processes, set priorities for review topics, participate in technical expert panels for commissioned evidence review topics, and develop and publish recommendations.

EGAPP Working Group (EWG) members reviewed the evidence report, key primary publications, other sources of information, and comments on the evidence report from the test developers. The process also included assessment of key gaps in knowledge and relevant contextual factors (e.g., availability of diagnostic or therapeutic alternatives, feasibility and practicality of implementation, and cost-effectiveness). The final EWG recommendation statement was formulated based on magnitude of effect, certainty of evidence, and consideration of contextual factors.

Rating Scheme for the Strength of the Recommendations

Recommendations Based on Certainty of Evidence, Magnitude of Net Benefit, and Contextual Issues

High or Moderate	Recommend for: • If the magnitude of net benefit is Substantial, Moderate, or Small, unless additional considerations warrant caution. • Consider the importance of each relevant contextual factor and its magnitude or finding. Recommend against: • If the magnitude of net benefit is Zero or there are net harms. • Consider the importance of each relevant contextual factor and its magnitude or finding.
Low	Insufficient evidence: • If the evidence for clinical utility or clinical validity is insufficient in quantity or quality to support conclusions or make a recommendation. • Consider the importance of each contextual factor and its magnitude or finding. • Determine whether the recommendation should be Insufficient (neutral), Insufficient (encouraging), or Insufficient (discouraging). • Provide information on key information gaps to drive a research agenda.

Teutsch SM, Bradley LA, Palomaki GE, Haddow JE, Piper M, Calonge N, Dotson WD, Douglas MP, Berg AO; EGAPP Working Group. The

Evaluation of Genomic Applications in Practice and Prevention (EGAPP) initiative: methods of the EGAPP Working Group. Genet Med. 2009 Jan;11(1):3-14.

Cost Analysis

Cost-effectiveness modeling studies in this area require updating with current venous thromboembolism risk estimates but are suggestive that routine Factor V Leiden/prothrombin testing is not cost-effective.

The 6 cost-effectiveness studies identified all used decision analytic models, which can provide support for further investigation of the utility of an intervention if the assumptions in the models are compatible with actual practice. The data ranges explored in the sensitivity analyses demonstrated the variables to which the cost-effectiveness of the interventions were most sensitive.

One group used decision analysis to assess the cost-effectiveness of testing for Factor V Leiden (FVL) and extending warfarin anticoagulation for 3 years or for life in carriers following a first venous thromboembolism (VTE) in a hypothetical cohort of 35-year-old women. If the rate of recurrence remained constant (7.3 percent/year), lifelong anticoagulation was the more cost-effective strategy incremental cost-effectiveness ratio [ICER] = $16,823/quality-adjusted life year [QALY]) when compared to no testing and 6 months of anticoagulation). Lifelong anticoagulation was less cost-effective in patient populations with low FVL prevalence, low risk of recurrent VTE, or risk factors for bleeding on anticoagulant therapy.

Another group used decision analysis to assess the cost-effectiveness of testing for FVL and 2 years of warfarin anticoagulation in carriers following a VTE in a hypothetical cohort of 60-year-old men. FVL testing with 2 years of anticoagulation for carriers was a cost-effective strategy (ICER = $12,833/QALY) when compared to no testing and 6 months of anticoagulation. However, this intervention was not cost-effective for individuals with a high risk of fatal bleeding on warfarin, low VTE recurrence rate, low anticoagulation efficacy, or low anticoagulation compliance.

Building on the previous study, the author employed the same model to assess the cost-effectiveness of testing for double heterozygosity, followed by 2 years of warfarin anticoagulation for doubly heterozygous individuals. Testing for both mutations was cost-effective (ICER = $13,624/QALY) when compared to no testing and 6 months of anticoagulation. Testing was not cost-effective for patient populations with a high bleeding risk, low double-heterozygote prevalence, low levels of pulmonary embolism or mortality, or low anticoagulation efficacy.

Another group assessed the cost-effectiveness of a hypercoagulability testing panel and warfarin anticoagulation for 6, 12, 18, 24, or 36 months, or for life, following an apparently idiopathic deep venous thrombosis (DVT) in a hypothetical cohort of 40-year-olds. In the base case analysis, extending anticoagulation for 24 months following a positive test was the most cost-effective option (ICER = $11,100/QALY) when compared to the least costly option of not testing and treating for 24 months. The authors concluded that tests detecting disorders present in at least 5 percent of the population that confer a relative risk exceeding 1.25, including FVL and prothrombin G20210A, should be included.

Another decision analysis with a 5-year time horizon assessed the effectiveness of extending anticoagulation from 3 months for FVL carriers and non-carriers following an initial lower-limb DVT to 1, 2, 3, 4, or 5 years in a hypothetical cohort. The authors stated that the risk of bleeding must be below 2.5 percent/year in order for prolonged anticoagulation to be the more effective strategy.

Finally, one group used a decision-analytic model with a 12-month time horizon to assess the cost-effectiveness of universal or selective screening for FVL and resultant changes in management for carriers in four cohorts at high risk of VTE. In all four cohorts, selective screening was more cost-effective than universal screening.

One group used the cost and outcomes data from a prospective cohort of 967 pregnant women in the United Kingdom to assess the cost-effectiveness of FVL testing and enoxaparin anticoagulant prophylaxis to prevent pregnancy-related vascular complications over the 8-month time horizon, from 12 weeks of gestation to 6 weeks postpartum. No women actually received anticoagulant prophylaxis, but the hypothetical impact of treating FVL carriers with an assumed efficacy of 50 percent was modeled. Testing only those women with a personal or family history of VTE was the most cost-effective approach.

Method of Guideline Validation

Not stated

Description of Method of Guideline Validation

Not applicable

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is not specifically stated for each recommendation.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Prevention of unnecessary genotyping for mutations associated with idiopathic venous thromboembolism (VTE)
- Not testing avoids potential net harm that could result if primary prophylaxis is administered to asymptomatic family members with one or more of these mutations, because the absolute risk of an initial VTE event is low, and the risk of anticoagulant-induced hemorrhage is relatively high.

Potential Harms

Not stated

Qualifying Statements

Qualifying Statements

- This recommendation statement is a product of the independent Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group. Although the Centers for Disease Control and Prevention (CDC) provides support to the EGAPP Working Group, including staff support in the preparation of this document, recommendations made by the EGAPP Working Group should not be construed as official positions of the CDC or the US Department of Health and Human Services.
- The research literature is insufficient in many respects, and the EGAPP Working Group (EWG) recommends further studies that could address important gaps in knowledge.
- It is speculated that absence of data on anticoagulation strategies for asymptomatic family members who are heterozygous for Factor V Leiden might be explained by an unfavorable risk/benefit balance because of low absolute risk for venous thromboembolism. This is not considered a gap in knowledge.
- The evidence report is based on research conducted by the Johns Hopkins University Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. HHSA 290-2007-10061-I). The findings and conclusions in this document are those of the author(s), who are responsible for its content, and do not necessarily represent the views of AHRQ. No statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Quick Reference Guides/Physician Guides

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Safety

Identifying Information and Availability

Bibliographic Source(s)

Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group. Recommendations from the EGAPP Working Group: routine testing for Factor V Leiden (R506Q) and prothrombin (20210G>A) mutations in adults with a history of idiopathic venous thromboembolism and their adult family members. Genet Med. 2011 Jan;13(1):67-76. [55 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2011 Jan

Guideline Developer(s)

Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group - Independent Expert Panel

Source(s) of Funding

United States Government

Guideline Committee

The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group

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Financial Disclosures/Conflicts of Interest

Steven Teutsch is a former employee and an option holder in Merck & Co., Inc.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Web site .

Also available in EPUB for eBook devices from the Genetics in Medicine Journal Web site .

Availability of Companion Documents

The following are available:

- Genetic tests for idiopathic venous thromboembolism: EGAPP™ recommendation. CDC summary of EGAPP recommendations. Electronic copies: Available from the Centers for Disease Control and Prevention Web site .
- Outcomes of genetic testing in adults with a history of venous thromboembolism. Evidence Report/Technology Assessment No. 180. (Prepared by the Johns Hopkins University Evidence-based Practice Center, Baltimore, MD under Contract No. HHSA 290-2007-10061-I.) AHRQ Publication No. 09-E011. Rockville (MD): Agency for Healthcare Research and Quality. 2009 Jun. 162 p. Electronic copies: Available from the Agency for Healthcare Research and Quality Web site .
- Predictive value of Factor V Leiden and prothrombin G20210A in adults with venous thromboembolism and in family members of those with a mutation. A systematic review. JAMA 2009 Jun 17;301(23):2472-85. Electronic copies: Available from the Journal of the American Medical Association Web site .
- Analytic validity of genetic tests to identify factor V Leiden and prothrombin G20210A. Critical review. Am J Hematol 2010 Apr;85(4):264-70. Electronic copies: Available from the American Journal of Hematology Web site .
- The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) initiative: methods of the EGAPP Working Group. 2009 Jan. 12 p. Available from the Genetics in Medicine Journal and the Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on May 3, 2011. The information was verified by the guideline developer on July 27, 2011.

Copyright Statement

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